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EXAMINER
PETERSEN

1SM2

GENENTECH, INC.
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ART UNIT	PAPER NUMBER
1806	17

DATE MAILED: 05/19/93

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 2/3/93 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-23 are pending in the application.
   Of the above, claims 14-16 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☒ Claims 12 and 13 are allowed.
4. ☒ Claims 1-11, 17-21 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Some of the rejections under 35 USC 112 second paragraph have been obviated in view of the amendments to the claims. However, the following rejection still remain. The language "consensus human variable domain" is still unclear despite the description in the specification. It is unclear whether the consensus human variable domain is a culmination of different variable domains or a single universal variable domain which is homologous to other human variable domains.

With regards to the langauge "import amino acid", it is suggested the import amino acid be described in the following manner: "an import antibody comprising the amino acid sequence of a non-human antibody which binds to ...". The language "reasonably expected" is unclear since it is not known what criteria determines what is "reasonable".

Claim 1 remains rejected and new claims 19-21 are rejected under 35 USC 112 first paragraph as lacking enablement for the language "at least a portion" for the same reasons as set forth in pages 3 and 4 of paper #13.

Applicant states that this language has been deleted from claim 1, but, this is not the case. This language has been moved to the beginning of the claim and the claim contains the same objectionalble language, therefore, the rejection set forth

previously still applies.

The rejection of claims 1-4, 6-8 under 35 USC 101 is withdrawn in view of the amendment to the claims.

The rejection of claims 9-13 as lacking utility is withdrawn in view of the argument set forth in the letter of 2/3/93.

The objection to the specification and the rejection of claims 1-11 under 35 USC 112 first paragraph is maintained and newly added claims 17-21 are rejected for the reasons of record.

The language "at least a portion" still remains in claim 1 and newly added claims 19-21. Therefore, the rejection set forth previously on pages 3-4 of paper #13 still applies. With regards to substituting an import CDR in place of the human CDR, the rejection still applies, since there is no clear guidance in the specification to enable one of ordinary skill in the art to make the human "consensus variable region" which is to contain the claimed substitution. It is true that once the amino acid sequences are known, it is routine to determine the CDRs according to Kabat, and substitute the rodent CDRs in place of the human CDRs. However, the only guidance presented in the specification with regards to the substitutions is the amino acid sequences of SEQ ID NO: 3 and 4, which are specific variable regions. The specification vaguely alludes to variable domain sequences which are derived from the most abundant subclasses but shows no way of making such variable domains. The fact remains

that applicant has not clearly taught how to determine which amino acids are the ones to be substituted since there is only a single example of the appropriate variable region which is to support the substitutions.

The rejection of claim 2 with regards to determining which residues are surface or buried residues is withdrawn in view of the argument presented explaining that computer modeling is well known in the art to determine the position of various amino acid residues.

The rejection of claims 1 and 3 with regards to the language "reasonably" and newly added claim 19 is maintained, since there is no set standard for determining what is reasonable interaction, or interfacing or what amount of glycosylation reasonably affects binding.

The rejection of claims 6,7 and 9 based on the specific amino acids sequences which are only relevant to IgG is maintained. Applicant argues that he is not required to exemplify every embodiment, however, if the claim requires the presence of a certain sequence which does not exist in a particular isotype, than clearly there is a lack of enablement for making that particular embodiment of the claim.

The rejections of claims 1,2,5-10 under 35 USC 102(a) and 102(b) is maintained and newly added claims 17-21 are rejected under 35 USC 102(a) and 35 USC 102(b) as being anticipated by

Queen et. al. or Co et. al. for the same reasons as set forth in the previous Office action.

Applicant argues that the distinction between the prior art and the instant invention is that the framework amino acids are chosen from a consensus human variable region. However, as previously mentioned there is no clear indication of what is meant by consensus variable regions and as it is stated by applicant on page 14 of the response the chosen amino acids in the references may indeed be the same as what applicant calls consensus variable domain sequences.

The rejection of claims 3 and 4 under 35 USC 103 is maintained for the same reasons as set forth in the previous Office action. Applicant again argues that the use of "consensus region variable domains" is different from the prior art methods, however, as previously mentioned, the consensus amino acids may be the same as the most homologous murine antibodies of the references. The lack of clarity of the language "consensus" amino acid region" is what allows this particular interpretation of the claims.

Claims 17,18, 20 and 21 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject, matter which applicant regards as the invention. New claims 17,18,20 and 21 are indefinite in that there are no discrete method steps.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lila Feisee whose telephone number is (703) 308-2731.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Feisee/em
May 18, 1993

DAVID L. LACEY
SUPERVISORY PATENT EXAMINER
GROUP 180
5/19/93